Certification Regarding Environmental Tobacco Smoke

Public Law 103–227, Part C—Environmental Tobacco Smoke, also known as the Pro-Children Act of 1994 (Act), requires that smoking not be permitted in any portion of any indoor routinely owned or leased or contracted for by an entity and used routinely or regularly for provision of health, day care, education, or library services to children under the age of 18, if the services are funded by Federal programs either directly or through State or local governments, by Federal grant, contract, loan, or loan guarantee. The law does not apply to children's services provided in private residences, facilities funded solely by Medicare or Medicaid funds, and portions of facilities used for inpatient drug or alcohol treatment. Failure to comply with the provisions of the law may result in the imposition of a civil monetary penalty of up to $1000 per day and/or the imposition of an administrative compliance order on the responsible entity.

By signing and submitting this application the applicant/grantee certifies that it will comply with the requirements of the Act. The applicant/grantee further agrees that it will require the language of this certification be included in any subawards which contain provisions for the children's services and that all subgrantees shall certify accordingly.

[FR Doc. 95–15585 Filed 6–23–95; 8:45 am]

BILLING CODE 4184–01–P

Food and Drug Administration

[Docket No. 95N–0182]

KV Pharmaceutical Co.; Proposal To Withdraw Approval of Two Abbreviated New Drug Applications and One Abbreviated Antibiotic Drug Application; Opportunity for a Hearing

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is proposing to withdraw approval of two abbreviated new drug applications (ANDA's) and one abbreviated antibiotic application (AADA) held by KV Pharmaceutical Co., 2503 South Hanley Rd., St. Louis, MO 63144 (KV). The grounds for the proposed withdrawals are (1) that the applications contain untrue statements of material fact; and (2) that based upon new information evaluated together with the evidence available when the applications were approved, there is a lack of substantial evidence that the drugs will have the effect they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

DATES: A hearing request is due on July 26, 1995; data and information in support of the hearing request are due August 25, 1995.

ADDRESSES: A request for a hearing, supporting data, and other comments should be identified with Docket No. 95N–0182 and submitted to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Harry T. Schiller, Center for Drug Evaluation and Research (HFD–366), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–2041.

SUPPLEMENTARY INFORMATION:

I. Background

On February 4, 1992, FDA attempted to inspect KV to determine whether or not the firm was following current good manufacturing practice (CGMP) regulations. The firm, however, refused to provide necessary records as required under the Federal Food, Drug, and Cosmetic Act (the act). (See sections 505(k) and 704 of the act (21 U.S.C. 355(k) and 21 U.S.C. 374).) The agency, therefore, obtained inspection warrants and inspected KV between March 11 and April 23, 1992. Despite the inspection warrants, KV failed to provide all of the documents requested. FDA conducted another inspection of KV between July 31 and November 3, 1992.

During the two 1992 inspections, the agency compared documents and data found at the firm with records previously submitted to FDA in support of KV's AADA and ANDA applications. The agency discovered that KV had submitted false and misleading information in the following applications:

1. AADA 62–047, Erythromycin Ethylsuccinate Oral Suspension, 200 and 400 milligrams (mg);

2. ANDA 71–929, Disopyramide Phosphate Extended Release Capsules, 100 mg; and

3. ANDA 86–538, Nitroglycerin Extended Release Capsules, 2.5 mg.

In support of the AADA and the two ANDA's listed above, KV submitted analytical data necessary for approval and continued approval of the applications, including stability data. During its inspections of KV, the agency discovered documents that showed that KV had made untrue statements in some of the stability data it had submitted in supplements and amendments to the applications. The documents also showed that KV had made untrue statements concerning stability data in annual reports submitted to the applications.

In letters dated June 1, 1993, and November 12, 1993, FDA informed KV that the agency intended to downgrade the therapeutic equivalency rating of the products listed above in the agency's publication ''Approved Drug Products with Therapeutic Equivalence Evaluations'' (the ''Orange Book'') and to begin the administrative procedures necessary to withdraw approval of the products. Accordingly, as explained below, the Director of the Center for Drug Evaluation and Research (the Director) is proposing to withdraw approval of the products' applications.

II. Evidence That the Applications Contain Untrue Statements of Material Fact

The first ground for withdrawing the AADA and two ANDA's listed above is that the applications contain untrue statements of material fact (21 U.S.C. 355(e)(5)). This section presents FDA's general comments on untrue statements and materiality, and then sets forth the specific false and misleading information in the three abbreviated applications.

A. Untrue Statements

The untrue statements submitted by KV in its drug applications include both stability test results that are inconsistent with stability test results retained by the firm and selective or incomplete reporting of stability date.

1. Conflicts Between Information Submitted to the Agency and Information Retained by the Firm

The first type of untrue statement submitted in the drug applications listed above consists of data that differ from data and other primary source information discovered at the firm. The agency concludes in such cases that, in the absence of a satisfactory explanation, the discrepant information in the application is untrue.

Information in an AADA or ANDA, including the facts and data covered by this notice, is generally derivative information. Such information is often a restatement, summary, or copy of original data or other underlying information such as that found in laboratory notebooks not specifically included in the application. The agency believes that original or underlying data generally have a higher degree of reliability because they are the primary sources of the information that are usually created contemporaneously with the event the information describes. Restated, summarized, or copied information submitted in the

application is transcribed, calculated, or otherwise derived from the original or underlying sources and is prepared after the events actually occurred and, therefore, is generally less reliable in the event of a discrepancy or inconsistency. Errors in the original or underlying data, even if discovered during the preparation of an application, should be corrected with a proper explanation.

2. Selective Reporting

The second type of untrue statement in the KV applications listed above consists of selective or incomplete reports of stability data. Selective reporting refers to reports that contain certain passing results only. Selective reporting does not consistently contain failing results and does not consistently contain a scientific justification for rejecting the failing data. Selective reporting thus misrepresents results, introduces bias into the studies' analysis, and may result in erroneous conclusions about the stability of the product.

B. Material Fact

KV's ANDA's and AADA, filed under sections 505(j), 505(b), and 507 of the act and implementing regulations, did not require for their approval the submission of animal toxicity studies, human safety studies, and adequate and well-controlled clinical effectiveness studies. Rather, the approval of an abbreviated application is based on a showing that the generic drug is equivalent to the innovator drug on certain key chemical and pharmacologic parameters, and, thus, will be therapeutically equivalent to the innovator drug throughout the shelf life of the generic product.

A finding that the generic and innovator drugs are chemically equivalent with respect to the active ingredient and bioequivalent with respect to the extent and rate of absorption of the active ingredient includes adequate proof that the generic product will remain stable throughout its labeled shelf life. Stability is demonstrated by showing that the drug product will remain within specifications established to ensure its identity, strength, quality, and purity throughout its specified shelf life. The stability data help, therefore, to provide assurance that a generic product will retain its physical, chemical, and bioequivalent characteristics throughout its labeled shelf life.

To obtain FDA approval, an application for a generic drug must demonstrate with reliable data and information (including stability data) that the generic drug is equivalent to the innovator drug so that the toxicity, safety, and effectiveness studies supporting the approval of the innovator drug also support approval of the generic drug. Moreover, FDA must have a reasonable basis on which to conclude that data based on test batches of a generic product are representative of the proposed commercial batches of that generic product.

To maintain continued approval of a drug, the sponsor must, among other things, comply with various post-marketing reporting requirements. Under 21 CFR 314.81, a sponsor must file annual reports, which then become a part of the application; the failure to file such annual reports may be grounds for withdrawing approval of the application.

A fact is material if it has the natural tendency to influence or be capable of affecting or influencing a government function. (See *U.S.* v. *Brittain*, 931 F.2d 1413, 1415 (10th Cir. 1991); *Gonzales* v. *United States*, 286 F.2d 118, 122 (10th Cir. 1960), *cert. denied*, 365 U.S. 878 (1961); *Weinstock* v. *United States*, 231 F.2d 699, 701–702 (D.C. Cir. 1956)). The statements submitted by KV about stability data are required information for the approval or continued approval of an ANDA or AADA (see 21 U.S.C. 355(j)(2)(A)(vi), 355(b)(1)(C), 355(b)(1)(D); 21 CFR 314.50(d)(1), 314.94(a)(9), 314.94(c), and 314.81).

Statements pertaining to stability are among the many statements in an abbreviated application on which FDA relies when deciding whether or not to approve an application for a generic product (see 21 U.S.C. 355(j)(3)(A) and 355(j)(3)(F); 21 CFR 314.94 and 314.125). Similarly, when allowing a proposed tentative expiration dating period, FDA relies on the manufacturer's written commitment in the application to conduct or continue shelf life stability studies on at least the first three production batches to establish the actual expiration dating period (see 21 CFR 314.94(a)(9), 314.94(c), and 314.50(d)(1)). Moreover, FDA relies on data submitted in annual reports to determine whether an application should continue to be approved (see 21 U.S.C. 355(e), 355(k); 21 CFR 314.81, 433.1).

Because the statements in the applications that are the subject of this notice were capable of affecting or influencing FDA's review of the applications, they are material.

C. Specific Untrue Statements of Material Fact Contained in Each Application

The specific untrue statements of material fact found in each application are described below. KV received written notice of many of these untrue statements in inspectional observations on Forms FDA–483 after FDA's inspections of March 11 through April 23, 1992, and July 31 through November 3, 1992.

1. AADA 62–047, Erythromycin Ethylsuccinate Oral Suspension, 200 and 400 mg

KV was not the original holder of this AADA. KV purchased the original holder and its approved applications, including AADA 62–047, the AADA for erythromycin ethylsuccinate oral suspension (EES). EES is a drug recognized in the United States Pharmacopeia (U.S.P.), and, therefore, the drug must meet the specifications regarding strength, quality, and purity prescribed in the U.S.P. unless the deviations are stated on the label. KV's EES product is labeled to indicate conformance with such U.S.P. specifications, not deviations.

On August 2, 1989, KV submitted to FDA two supplements to AADA 62–047, seeking approval for manufacturing changes (supplement S–006 for its 200 mg EES and supplement S–007 for its 400 mg EES). After evaluating KV's submissions, FDA issued a deficiency letter on September 14, 1989, regarding a number of issues, including KV's failure to provide adequate stability data for EES manufactured by KV's proposed new process. KV amended these supplements on August 14, 1990, and again on December 19, 1990. FDA approved the supplements in a letter dated April 12, 1991.

Subsequently, during the inspections of March 11 through April 23, 1992, and July 31 through November 3, 1992, FDA compared the data submitted in these supplements with records found at the firm. The comparisons demonstrated that the data submitted in response to FDA's 1989 deficiency letter omitted failing stability results and falsely reported failing results as passing. These data were false and misleading and material to the approval of the AADA supplements.

In the August 14, 1990, amendment to its then pending AADA supplement, KV provided results from freeze/thaw cycle stability studies for lot L2072 (200 mg) and lot L2071 (400 mg), which were performed by an independent contractor. Records discovered at KV, however, showed that KV did not report failing freeze/thaw results done by KV's lab. The selectively reported data submitted to FDA are misleading because they do not reflect all of the stability testing results of the lots, and,

thus, constitute untrue statements of material fact.

In the August 14, 1990, amendment to its then pending supplement, KV also selectively reported only a passing result for a 12-month stability test for lot L2071 (400 mg) for methylparaben, an inactive ingredient, although KV's records showed an initial unreported result in which the lot failed to meet the firm's specifications approved in the AADA for methylparaben.

In the August 14, 1990, amendment to its then pending supplement, KV falsely reported that lot L2072 (200 mg) passed a 6-month stability test for methylparaben. However, KV's records for the same time and storage conditions showed that L2072 failed to meet the firm's specifications as approved in the AADA.

FDA's inspection also established that KV made untrue statements in certain annual reports by submitting false stability study results and by omitting failing stability results for EES 200 mg and 400 mg. In KV's April 30, 1991, annual report for its 200 mg EES product, the firm falsely stated that lot L2510 passed an erythromycin assay at 3 months. However, records from the outside contract laboratory that conducted the 3-month assay show that the erythromycin assay results for lot L2510 were below the U.S.P. specifications.

In KV's September 26, 1991, annual report for EES 400 mg, the firm falsely reported that the assay of the active ingredient in lot L2071 passed stability testing at 18 months. Records at the firm, however, showed that lot L2071 failed testing at 18 months because the results were below U.S.P. specifications.

Records from KV show that EES lot L1791 (200 mg) failed assays for erythromycin and for an inactive ingredient at 18 months. KV, however, did not report these failures in its April 30, 1991, annual report as required under 21 CFR 314.81. On April 28, 1992, KV recalled both strengths of EES because of recurrent stability problems. Only after this recall, in the firm's June 2, 1992, annual report, did KV report the stability test failures of EES lot L1791.

The stability failures in 1990 and 1991 were capable of affecting FDA's continued approval of the AADA because they provide evidence directly relevant to the product's safety and effectiveness. KV's omission in the April 30, 1991, annual report of the available information about the 1990 and 1991 failures misrepresented the product's quality at that time and, therefore, the applications contain untrue statements of material fact.

2. ANDA 71–929, Disopyramide Phosphate Extended Release Capsules, 100 mg

FDA's inspections of KV revealed that the firm made untrue statements about the stability of its Disopyramide Phosphate Extended Release Capsules (100 mg) in its September 10, 1992, annual report, as explained below. Disopyramide Phosphate Extended Release Capsules must meet the specifications regarding strength, quality, and purity prescribed in the approved ANDA, as amended. The stability data submitted in the annual reports and discussed below are false and misleading and are material to the continued approval of the ANDA application.

First, KV reported that in December 1991, lot V1040 passed ANDA specifications for 18-month drug release testing at 1, 4, and 8-hour intervals. Records at the firm, however, showed that the six capsules tested by KV on December 11, 1991, failed the 4-hour test both individually and collectively. These failing data were lined through and the notation ''Inconsistent with history and retest'' was added. No other notation or explanation of KV's December 11, 1991, test results was recorded. KV did not report this failure in the September 10, 1992, annual record or record an explanation for omitting this failure from the annual report. Five days later, on December 16, 1991, KV tested another six capsules, which passed the 4-hour specifications. KV selectively reported only the average of the passing test results in the annual report, and the omission of failing data in the annual report was misleading.

KV also reported in the September 10, 1992, annual report that in April 1991, the 3-month drug release test for lot V1377 passed ANDA specifications at the 4-hour interval. Records at the firm, however, showed that on April 18, 1991, the aggregate average value of the six capsules tested was below drug release specifications for the 4-hour interval. Five of the six individual capsules were also below specifications at 4 hours. These failing data were not reported in the September 10, 1992, annual report.

Four months later, on August 18 and 19, 1991, KV reassayed the lot three times and selectively reported only the results from the first reassay. Furthermore, in the September 10, 1992, annual report, KV falsely reported that the drug release test result had been obtained at 3 months, but KV's records showed that it had been obtained at 7 months.

KV also reported in the September 10, 1992, annual report that lot V1497 passed both 4 and 8 hour, 12-month drug release tests in May 1992. KV's records, however, showed that a set of six capsules failed the 8 hour, 12-month ANDA drug release test on July 21, 1992. On August 3, 1992, a second set of six capsules passed both 4 and 8 hour drug release tests. However, these results were crossed out on the firm's stability data report form. A handwritten note next to these results reads ''Void. See recal using correct shell factor.'' On August 8, 1992, KV recalculated both the 4-hour and 8-hour drug release test results. The aggregate averages for both 4 hour and 8 hour tests passed specifications. However, two of the six capsules failed at 4 hours and two of the six capsules failed at 8 hours. The notation ''Recal'' is written beside this third set of data. KV selectively reported only the passing 4 and 8 hour aggregate average results in the September 1992, annual report.

3. ANDA 86–538, Nitroglycerin Extended Release Capsules, 2.5 mg

FDA's inspections of KV revealed that the firm made untrue statements in certain annual reports about the stability of its Nitroglycerin Extended Release Capsules. These untrue statements consisted of false reporting and selective reporting of stability data, including content uniformity data, which are material to the continued conditional approval of the application.

In its April 29, 1988, annual report, KV reported that on July 28, 1987, the content uniformity test data for lot V8715 were not available at 24 months. KV's records, however, included content uniformity test results for this lot, which showed that lot V8715 failed to meet U.S.P. specifications at 24 months. Although Nitroglycerin Extended Release Capsules is not listed in the U.S.P., the standard test for content uniformity of any product is described in the U.S.P., and KV's submissions stated that it met the U.S.P. test.

In its June 6, 1989, annual report, KV reported that the 12-month assay for nitroglycerin in lot V8648 tested within the ANDA specifications. KV's records, however, showed that an assay result was outside the ANDA assay limits. The passing result KV reported was an average of the failing result and two additional assays it performed.

In the June 6, 1989, annual report, KV reported that a nitroglycerin assay purportedly conducted at 9 months after lot V9527 was within ANDA specifications. KV's records, however, showed that the KV lab test result,

which was dated March 3, 1988, failed to meet ANDA specifications. KV records also showed that the stability test result KV reported in its annual report was the average of two retests performed by KV on April 19, 1988.

In the June 6, 1989, annual report, KV falsely reported that lot V9133 conformed to U.S.P. specifications in a content uniformity test conducted 6 months after the lot was manufactured. KV's records, however, showed that the first 10 capsules of the lot failed U.S.P. relative standard deviation (RSD) specifications and contained no evidence that KV tested an additional 20 capsules. Without further testing of an additional 20 capsules, the batch failed to meet U.S.P. specifications. Therefore, lot V9133 did not conform to U.S.P. specifications.

In its May 8, 1990, annual report KV reported that lot V9432 passed a 24-month stability test in April 1989. Records at the firm, however, show that the lot failed its stability test on May 15, 1989. During retesting on June 5, 1989, the lot passed stability testing and met assay specifications twice. KV averaged the passing tests and then improperly averaged that resultant average with the failing result. This final average was reported as a passing result in the May 8, 1990, annual report.

KV reported in its May 8, 1990, annual report that lot V9527 met ANDA assay specifications, purportedly in an 18-month stability test of nitroglycerin conducted in February 1989. Records at the firm, however, show that the lot failed the first stability test on May 15, 1989. The lot passed the second and third stability tests, done on June 5, 1989. KV improperly averaged the three test results and reported in the annual report the average as a passing result. Furthermore, the retests were conducted 21 and 22 months after the batch was manufactured, but KV reported in the annual report that the tests were conducted at 18 months.

KV reported in an August 6, 1992, letter to the agency that lot V9991 passed the 24-month content uniformity test and conformed to U.S.P. specifications. Records at the firm, however, showed that the group of capsules tested failed because its RSD was above U.S.P. RSD specifications. In addition, the results of two individual capsules were below U.S.P. specifications. According to U.S.P. specifications, such failing results require testing an additional 20 capsules, which KV did not do. Therefore, this lot did not conform to U.S.P. specifications.

KV reported in an August 1, 1990, supplement that lot V9527 passed a 12-month stability test for nitroglycerin. Records at the firm, however, show that the lot failed a stability test on September 22, 1988, and thus did not meet the ANDA assay specifications. KV then conducted two retests on October 4, 1988. KV selectively reported the result of only one of the passing retests, and also falsely reported the date of the test as August 15, 1988, which was 2 months before the actual test date.

D. Conclusion

On the basis of the foregoing findings, the Director finds that KV submitted untrue statements of material fact in the AADA and two ANDA's listed above, and, therefore, proposes to withdraw the approval of these applications under section 505(e)(5) of the act.

III. Evidence That the Drugs Lack Substantial Evidence of Effectiveness

Sction 505(e)(3) of the act provides that approval of an AADA or an ANDA shall be withdrawn if, on the basis of new information, evaluated together with the evidence available when the application was approved, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have. Because KV submitted untrue statements regarding the stability of its product in annual reports, supplements, and amendments to its applications, the agency cannot be assured of the products' stability. Moreover, the agency can no longer be assured as to the accuracy and validity of any of the data used to support approval and continued approval of these applications. Thus, the discovery of these untrue statements constitutes new information demonstrating that there is a lack of substantial evidence that the drugs will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

The reliability of stability data is of particular concern when, as here, the results of multiple stability tests, both reported and unreported, indicate a significant history of stability problems. Without reliable stability data, FDA cannot be assured that a drug will maintain the efficacy upon the basis of which the drug was approved. Similarly, in the case of stability problems with generic drugs, FDA cannot be assured that the drug will continue to be bioequivalent to the innovator drug over a given period of time. In either case, an unstable drug product may be more or less potent than the efficacy parameters that the agency approved.

Because there are no reliable data or information to demonstrate the stability and bioequivalence of these products to the listed drugs, the three products listed above lack substantial evidence of effectiveness.

IV. Proposed Action and Notice of Opportunity For a Hearing

The Director has evaluated the information discussed above concerning the filing of untrue statements of material fact by KV and, on the grounds stated, is proposing to withdraw approval of the following AADA and ANDA's:

1. AADA 62–047, Erythromycin Ethylsuccinate Oral Suspension, 200 and 400 mg;
2. ANDA 71–929, Disopyramide Phosphate Extended Release Capsules, 100 mg; and
3. ANDA 86–538, Nitroglycerin Extended Release Capsules, 2.5 mg.

Notice is hereby given to the holder of the AADA and ANDA's listed above and to all other interested persons that, based upon the information discussed above concerning the filing of untrue statements by KV and, on the grounds stated, the Director proposes to issue an order under section 505(e) of the act withdrawing approvals, including conditional approvals, of the foregoing AADA and ANDA's, and all amendments and supplements thereto. The Director finds that: (1) The applications contain untrue statements of material fact; and (2) on the basis of new information before her with respect to the drugs, evaluated together with the evidence available to her when the applications were approved, there is a lack of substantial evidence that the drugs will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

In accordance with section 505(e) of the act and 21 CFR part 314, the applicant is hereby given an opportunity for a hearing to show why approval of the AADA and ANDA's should not be withdrawn.

An applicant who decides to seek a hearing shall file: (1) On or before July 26, 1995, a written notice of appearance and request for a hearing, and (2) on or before August 25, 1995, the data, information, and analyses relied on to demonstrate that there is a genuine issue of material fact to justify a hearing. Any other interested person may also submit comments on this notice. The procedures and requirements governing this notice of opportunity for a hearing, a notice of appearance and request for a hearing, submission of information

and analyses to justify a hearing, other comments, and a grant or denial of a hearing, are contained in 21 CFR 314.200 (except that the limitations imposed by 21 CFR 314.200(d)(1) and (d)(2) do not apply) and in 21 CFR part 12.

The failure of the applicant to file a timely, written notice of appearance and request for a hearing, as required by 21 CFR 314.200, constitutes an election by that person not to use the opportunity for a hearing concerning the action proposed, and a waiver of any contentions concerning the legal status of that person's drug products. Any new drug product marketed without an approved new drug application is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must present specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. In order to raise a genuine and substantial issue of fact justifying a hearing on the issue of whether the application contains untrue statements, the applicant must specifically identify new evidence that supports its position. Mere allegations and denials, arguments by counsel, or the unsupported articulation of possible alternate inferences will not suffice to obtain a hearing. See 21 CFR 12.24(b)(2); see also *Cooper Laboratories, Inc.* v. *Commissioner, Federal Food and Drug Administration,* 501 F.2d 772, 785 (D.C. Cir. 1974); *Pineapple Growers Ass'n* v. *Food and Drug Administration,* 673 F.2d 1083–1085 (9th Cir. 1982); *Weinberger* v. *Hynson, Westcott & Dunning, Inc.,* 412 U.S. 609, 620–621 (1973).

In order to obtain a hearing, the new evidence must do more than reaffirm the applicant's belief that the information in the application is true. As explained above, the Director's conclusion that the applications contain an untrue statement of material facts is based on: (1) Selective reporting of stability data without justification, (2) omission of failing stability test results, and (3) actual conflicts between stability data reported to FDA and stability data retained by the firm.

In order to raise an issue of fact about whether the application contains truthful information, the applicant's evidence should be directed toward the basis of the Director's conclusion that the statements in the application are untrue. The applicant's failure to present evidence identifying a genuine and substantial issue of fact with respect to the Director's conclusion that the applications listed in this notice contain untrue statements of material fact, leaves the basis for the conclusion intact, and will result in the denial of a hearing on those issues.

In addition, the submission of truthful information to replace untrue statements will not result in a finding that the previously identified untrue statements are no longer material. If corrective information could nullify the materiality of untrue statements, then applicants could simply correct all untrue statements as soon as they were discovered.

Should a hearing be held on these issues, the participants requesting the hearing will bear the burden of proof with respect to whether the applications contain untrue statements of material fact and, ultimately, whether the drugs that are the subject of the applications listed in this notice have been shown to be safe and effective (21 CFR 12.87(d)).

If it conclusively appears from the face of the data, information, and factual analyses in the request for a hearing that there is no genuine and substantial issue of fact that precludes the withdrawal of approval of the applications, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who request the hearing, making findings and conclusions, and denying a hearing.

Section 505(j)(6)(C) of the act requires that FDA remove from its approved product list contained in FDA's publication the Orange Book any drug that was withdrawn for grounds described in the first sentence of section 505(e) of the act. If the agency determines that withdrawal of the drugs subject to this notice is appropriate, FDA will announce the removal of the relevant drugs from the list in the **Federal Register** notice announcing the withdrawal of approval of the drugs.

All submissions pursuant to this notice of opportunity for hearing are to be filed in four copies. Except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, the submissions may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (sec. 505 (21 U.S.C. 355)) and under authority delegated to the Director of the Center for Drug Evaluation and Research (21 CFR 5.82).

Dated: June 13, 1995.

Murry A. Lumpkin,

Deputy Director, Center for Drug Evaluation and Research.

[FR Doc. 95–15539 Filed 6–23–95; 8:45 am]

BILLING CODE 4160–01–P

National Institutes of Health

National Heart, Lung, and Blood Institute; Notice of a Closed Meeting

Pursuant to Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following Heart, Lung, and Blood Special Emphasis Panel (SEP) meeting:

Name of SEP: Lung Specific Drug Delivery Systems for Tuberculosis Treatment.

Date: July 18, 1995.

Time: 8:00 a.m.

Place: Hyatt Regency, Bethesda, Maryland.

Contact Person: Carl A. Ohata, Ph.D., 6701 Rockledge Drive, Room 7198, Bethesda, Maryland 20892–7924, (301) 435–0297.

Purpose/Agenda: To review and evaluate grant applications.

The meeting will be closed in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. Applications and/or proposals and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications and/or proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Programs Nos. 93.837, Heart and Vascular Diseases Research; 93.838, Lung Diseases Research; and 93.839, Blood Diseases and Resources Research, National Institutes of Health.)

Dated: June 19, 1995.

Susan K. Feldman,

Committee Management Officer, NIH.

[FR Doc. 95–15561 Filed 6–23–95; 8:45 am]

BILLING CODE 4140–01–M

National Institute of Dental Research; Notice of Closed Meetings

Pursuant to Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following National Institute of Dental Research Special Emphasis Panel (SEP) meetings:

Name of SEP: National Institute of Dental Research Special Emphasis Panel-Delivery System for Periodontal Tissue Growth Factors (Telephone Review).

Dates: July 6, 1995.

Time: 12:00 noon.

Place: Natcher Building, Rm. 4AN–44F, National Institutes of Health, Bethesda, MD 20892.

Contact Person: Dr. George Hausch, Chief, Review Section, 4500 Center Drive, Natcher Building, Room 4AN–44F, Bethesda, MD 20892, (301) 594–2372.

Purpose/Agenda: To evaluate and review grant applications and/or contact proposals.

Name of SEP: National Institute of Dental Research Special Emphasis Panel-PT Intervention-An Effective Change Agent in TMD (Telephone Conference).